

**AMENDMENTS TO THE CLAIMS**

selected SEQ ID NO: 1 +  $\Delta$ -4 desaturase

# election?  
species

is it a  
fusion  
polypeptide

- ① (currently amended) An isolated nucleic acid sequence which encodes a polypeptide and which is composed of a combination of the nucleic acid sequences of a biosynthetic nucleic acid sequence encoding of the a fatty acid or lipid metabolism enzyme and one of the following nucleic acids:

1. a nucleic acid sequence with the sequence shown in SEQ ID NO: 1,
2. nucleic acid sequences which are derived from the nucleic acid sequence shown in SEQ ID NO: 1 as the result of the degeneracy of the genetic code,
3. derivatives of the nucleic acid sequence shown in SEQ ID NO: 1 which encode polypeptides with the amino acid sequences shown in SEQ ID NO: 2 and which have at least 60% homology at the amino acid level, — function!
4. a nucleic acid sequence with the sequence shown in SEQ ID NO: 3 or the amino-terminal portion of the coding region of the sequence. } objected

- ② (currently amended) An isolated nucleic acid sequence as claimed in claim 1, wherein a sequence of the following protein groups is used as biosynthesis gene nucleic acid sequence of the fatty acid or lipid metabolism[[]] :

→ makes  
no sense

Acyl-CoA dehydrogenase(s), Acyl-ACP[=acyl carrier protein] desaturase(s), Acyl-ACP thioesterase(s), fatty acid acyltransferase(s), fatty acid synthase(s), fatty acid hydroxylase(s), acetyl-coenzyme A carboxylase(s), acyl-coenzyme A oxidase(s), fatty acid desaturase(s), fatty acid acetylenases, lipoxygenases, triacylglycerol lipases,

SID 1 = 732 CDS = 1-732

3 = 2964

allenoxide synthases, hydroperoxide lyases and/or fatty acid elongase(s).

- ③ (currently amended) An isolated nucleic acid sequence as claimed in claim 1, wherein a sequence of the following protein groups is used as biosynthesis ~~gene~~ nucleic acid

sequence of the fatty acid or lipid metabolism:

*make no sense*

fatty acid acyltransferase(s),  $\Delta 4$  desaturase,  $\Delta 5$  desaturase,  $\Delta 6$  desaturase,  $\Delta 9$  desaturase,  $\Delta 12$  desaturase,  $\Delta 15$  desaturase or a fatty acid elongase.

- ④ (currently amended) An isolated nucleic acid sequence as claimed in claim 1, wherein the derivatives mentioned under (c) have a homology at the amino acid level of 70%, preferably 80%[[, especially preferably of 90%]], over the entire region of the sequence shown in SEQ ID NO: 2 (~~Program Pilep, J. Mol. Evolution., 25, 351-360, 1987, Higgins et al., CABIOS, 5 1989: 151-153).~~

- W 5. (original) An amino acid sequence encoded by a nucleic acid sequence as claimed in claim 1.

- ⑥ (currently amended) An isolated nucleic acid construct comprising a nucleic acid sequence as claimed in claim 1, wherein the nucleic acid sequence is linked to one or more regulatory signals.

W 7. (previously presented ) The use if a nucleic acid sequence as claimed in claim 1 or of a nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals for the generation of transgenic plants.

8. (previously presented ) A vector comprising a nucleic acid sequence as claimed in claim 1 or a nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals. ~~which is a phage~~

9. (original) A vector as claimed in claim 8, which is a linear or circular DNA, a phage, a virus, a transposon, a IS element, a phasmid, a phagemid, a cosmid or a plasmid.

10. (currently amended) An organism comprising at least one isolated nucleic acid sequence as claimed in claim 1, at least one isolated nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals or at least one vector comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals or a nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals.

*Ready on human* → *Transgenic human*  
*Cucumis sativus*

101 & 112 enable  
ment

- ⑪ (original) An organism as claimed in claim 10, which is a eukaryotic organism.
- ⑫ (previously presented ) An organism as claimed in claim 10, which is a plant, a eukaryotic microorganism or an animal.
- ⑬ (previously presented) An organism as claimed in claim 10, which is a plant, a fungus or a yeast.
- ⑭ (currently amended) An organism as claimed in claim 10, which is ~~Yarrowia lipolytica, Saccharomyces cerevisiae, Traustochytrium, Arabidopsis thaliana, Brassica napus or Linum usitatissimum~~ Yarrowia lipolytica, Saccharomyces cerevisiae, Traustochytrium, Arabidopsis thaliana, Brassica napus or Linum usitatissimum.
- W 15. (previously presented ) A transgenic plant comprising a nucleic acid sequence as claimed in claim 1 or a nucleic acid construct comprising said nucleic acid sequence.

- W
16. (previously presented ) A method of targeting proteins involved in lipid or fatty acid biosynthesis into liposomes or lipid bodies, which comprises combining the protein-encoding nucleic acids and one of the following sequences to give a joint protein-encoding sequence:
1. a nucleic acid sequence with the sequence shown in SEQ ID NO: 1,
  2. nucleic acid sequences which are derived from the nucleic acid sequence shown in SEQ ID NO: 1 as the result of the degeneracy of the generic code,
  3. derivatives of the nucleic acid sequence shown in SEQ ID NO: 1 which encode polypeptides with the amino acid sequences shown in SEQ ID NO: 2 and which have at least 60% homology at the amino acid level,
  4. a nucleic acid sequence with the sequence shown in SEQ ID NO: 3 or the amino-terminal portion of the coding region of this sequence, and introducing the resulting sequence into a eukaryotic organism.
- W
17. (previously presented ) A method of targeting proteins involved in lipid or fatty acid biosynthesis into liposomes or lipid bodies, which comprises introducing at least one nucleic acid sequence as claimed in claim 1 or at least one nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals into an oil-producing organism.

- W
18. (previously presented ) A method of producing fatty acids or lipids, which comprises introducing at least one nucleic acid sequence as claimed in claim 1 or at least one nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals into an oil-producing organism, growing this organism and isolating the oil contained in the organism.
19. (previously presented ) A method of producing fatty acids, which comprises introducing at least one nucleic acid sequence as claimed in claim 1 or at least one nucleic acid construct comprising said nucleic acid sequence wherein the nucleic acid sequence is linked to one or more regulatory signals into an oil-producing organism, growing this organism, isolating the oil contained in the organism and liberating the fatty acids.
- W
20. (previously presented ) A method as claimed in claim 16, wherein the organism is a plant or a eukaryotic microorganism.

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### DETAILED ACTION

This application is a 371 of PCT/EP00/09912.

The amendment filed on May 11, 2006, amending claims 1-4, 6, 10 and 14, has been entered.

Claims 1-20 are pending. Claims 5, 7 and 15-20 are withdrawn. Claims 1-4, 6 and 8-14 are under consideration.

### Response to Arguments

Applicant's amendment and arguments filed on May 11, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### Claim Objections

Claim 1 is objected to because the claim is drawn to non-elected product SEQ ID NO:3.

Applicants traverse the objection arguing that SEQ ID NO:3 is the same as SEQ DI NO:1 except that it contains a 3'-5'-UTR and that this untranslated region does not qualify SEQ ID NO:3 as a separate invention. Examiner disagrees. Contrary to applicant's statement, SEQ ID NO:3 does not differ from SEQ DI NO:1 <sup>Just by comprising or 5'</sup> ~~except a 3'-5'~~ <sub>sequences.</sub> UTR. The polynucleotide of SEQ ID NO:3 is composed of 2684 nucleotides encoding a polypeptide having 878 amino acids. <sup>(See sequence listing)</sup> The polynucleotide of SEQ ID NO:1 is composed

The specification does not clearly indicate that SEQ ID NO:3

encodes ~~the~~ only the polypeptide SEQ ID NO:2  
Just as SEQ ID NO:1.

I doubt your arguments

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of 732 nucleotides encoding a polypeptide having 244 amino acids. The encoded polypeptides of SEQ ID NO:1 and 3 do not share special technical feature because the encoded proteins have different enzymatic activity and unrelated structure. Hence the objection is maintained.

Claims 2-3 are objected to because the claims are drawn to non-elected products Acyl-coA dehydrogenases, Acyl-ACP(=acyl carrier protein) desaturases, Acyl-ACP thioesterases, fatty acid acyltransferases, fatty acid synthases, fatty acid hydroxylases), acetyl-coenzyme A carboxylases, acyl-coenzyme A oxidases, fatty acid acetylenases, lipoxygenases, triacylglycerol lipases, allenoxide synthases, hydroperoxide lyases and/or fatty acid elongases, fatty acid acyltransferases, 5-desaturase, 6-desaturase, 9-desaturase, 12-desaturase, 15-desaturase and a fatty acid elongase.

Applicants have traversed the above objection arguing the objection is improper because the sequences of the fatty acid synthesis recited in claims 2-3 are elected products because they specify the nucleic acid sequence part of the fusion protein.

Examiner respectfully disagrees. As discussed in the Restriction Requirement mailed on April 14, 2004, requirement for further election of ONE biosynthesis gene of a fatty acid or lipid metabolism was not an election of species.

~~but a restriction.~~ The nucleic acid sequence construct comprising SEQ ID NO:1 and a biosynthesis gene of a fatty acid or lipid metabolism are independent chemical entities and require independent search in the patent and non-patent literature. The constructs express proteins having different enzymatic activity and unrelated structure. Further, the fatty acid or lipid metabolism

NOT clear.  
Was it a restriction



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genes recited in claims 2 and 3 do not share a special technical feature because the encoded proteins have different enzymatic activity and different and/or unrelated structure. The desaturase genes recited in claim 3 do not share a special technical feature because the encoded proteins have different function, substrate specificity, and different structure. Hence the objection is maintained.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 10-14, ~~as written, do not sufficiently distinguish over organisms comprising a polynucleotide of SEQ ID NO. 1 as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980).~~

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that amendment of claim 10 has overcome the rejection.

Examiner respectfully disagrees.

~~The claims also read on a human being comprising a~~ <sup>transferred with</sup> ~~polynucleotide of SEQ ID NO:1 linked to regulatory sequences.~~

"If the broadest reasonable interpretation of the claimed invention as a whole

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encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter". Hence the rejection is maintained.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-4, 6, 8-9 and 10-14 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the phrase <sup>encodes a polypeptide and</sup> ~~composed of a combination~~ is unclear. It is not clear to the Examiner if the nucleic acid sequence is a chimeric sequence comprising linked sequences encoding <sup>a fusion polypeptide and if so what is the final activity of each</sup> ~~enzymes of "fatty acid or lipid metabolism" and SEQ ID NO. 1, a~~ <sup>a polypeptide</sup> ~~polynucleotide encoding a fusion protein comprising enzymes of "fatty acid or lipid metabolism" and SEQ ID NO. 2 or a polynucleotide encoding enzymes of "fatty acid or lipid metabolism" and SEQ ID NO. 1, expressed with one or more expression regulatory sequences or that these sequences are simply combined together without a physical linkage between each other. For the rejection under 35 U.S.C. 103(a), the claim has been interpreted as a polynucleotide encoding a fusion protein.~~

Further more claim 1 also recites "biosynthetic nucleic acid seq.". The metes and bounds are unclear. Examiner suggests deletion of the term "biosynthetic".

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In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that amendment of claim 10 has overcome the rejection. Examiner respectfully disagrees. It is still unclear to the Examiner what applicants mean by "composed of a combination", if the claim is drawn to a chimeric sequence, a polynucleotide encoding a fusion protein or polynucleotide sequence simply combined together without a physical linkage between each other. Hence the rejection is maintained.

*Should not do this here since they also have ~60% homology in the claim.*

Claim 1 and claims 2-4, 6, 8-9 and 10-14 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "derivatives". The metes and bounds of this phrase is not clear to the Examiner. Literally, the term "derivatives" means a substance made from another substance. Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean that "derivatives" of the SEQ ID NO:1 are any variants or mutants of SEQ ID NO:1.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that "derivatives" is clearly defined in the specification. Examiner respectfully disagrees. The specification discloses one example of a

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definition for "derivatives", and does not exclude other interpretation. Therefore, "derivatives" of SEQ ID NO:1 are any variants or mutants of SEQ ID NO:1 retaining the activity of SEQ ID NO:1 or having any activity. Hence the rejection is maintained.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 2-3, the phrase "a sequence of the following protein groups is used" is unclear. It is not clear to the Examiner if the phrase "sequence" is referring to a sequential order of the recited genes in the polynucleotides or if the phrase "sequence" is referring to a nucleic acid "sequence" or the amino acid sequence of the protein. It is also not clear as to how nucleic acid sequences can be linked to amino acid sequences.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that the above phrase is defined in the specification. Examiner respectfully disagrees. The phrase is not defined in the specification (page 10). Further, it is still not clear to the Examiner how the nucleic acid sequence of claim 1 can be linked to an amino acid sequence of claim 2. Hence the rejection is maintained.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 4, the limitation "(c)" in line 2 is unclear because claim 1 does not recite "(c)". Hence the rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6 and 8-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of fusion polynucleotides comprising a polynucleotide encoding an enzyme involved in lipid or fatty acid metabolism and a polynucleotide with SEQ ID NO:1 encoding a polypeptide having 60% or 80% amino acid sequence identity with SEQ ID NO:2.

The specification does not contain any disclosure of the function of all fusion polynucleotide sequences encoding fusion polypeptides comprising amino acid sequences that are 60% or 80% identical to SEQ ID NO:2. The genus of these polynucleotides that comprise these above polynucleotide molecules is a large variable genus with the potentiality of encoding ~~many different~~ *with different functions* proteins. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims, including partial polynucleotide sequences. The specification discloses only a single species of the claimed genus (i.e. a polypeptide with SEQ ID NO:2 having lipid).

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body lipxygenase activity) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus including the fusion proteins. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that the claims meet the written description requirement because one of ordinary skill in the art would be able to arrive at sequences having 80% homology, by using computer programs. Examiner respectfully disagrees. First, the claims are also drawn to polynucleotides having 60% sequence identity to SEQ ID NO:1. Second, while one of ordinary skill in the art would be able to arrive at a polynucleotide having 80% sequence identity to SEQ ID NO:1, the genus comprising polynucleotides having 60-80% sequence to SEQ ID NO:1 encoding polypeptides having unknown activity or no activity is widely divergent. The specification does not describe the function of all the polypeptide sequences derived or modified from SEQ ID NO:1 and therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice,

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reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, **by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.** A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genus of the claims includes species which are widely variant in function. The genus of the claims is functionally diverse as it encompasses polynucleotides encoding polypeptides with LBLOX activity, those which lack such activity and those with no activity. As such, the description of solely structural features present in all members of the genus is <sup>not</sup> sufficient to be representative of the attributes and features of the entire genus. Hence the rejection is maintained.

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Claims 1-4, 6 and 8-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a fusion protein comprising the LBLOX of SEQ ID NO:2 and the fatty acid/lipid metabolism enzyme,  $\Delta$ -4 desaturase, wherein the fusion polypeptide continues to have LBLOX activity, does not reasonably provide enablement for a polynucleotide comprising any polynucleotides encoding any enzyme involved in fatty acid/lipid metabolism and a variant or mutant of SEQ ID NO:1 encoding a polypeptide having at least 60 or 80% amino acid sequence identity to SEQ ID NO:2, wherein the encoded polypeptide of SEQ ID NO:1 has any function or no function at all, vectors and transformed host cells comprising the above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. (see rejection under 35 U.S.C. 112, 2<sup>nd</sup> paragraph for interpretation of "derivative" of SEQ ID NO:1).

*what is the specific activity in biochemical terms.*

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1-4, 6 and 8-14 are directed to a fusion polynucleotide comprising a polynucleotide encoding an enzyme involved in fatty acid/lipid metabolism and a variant,



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mutant or recombinant of SEQ ID NO:1 encoding a polypeptide having at least 60%, 70%, 80% or 90% amino acid sequence identity to SEQ ID NO:2, vectors comprising said polynucleotide and organisms comprising said polynucleotide. Therefore, these claims are drawn to a genus of polynucleotides having any structure.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides comprising, variants and mutants broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a polynucleotide encoding a fusion protein comprising a specific fatty acid/lipid metabolism enzymes such as  $\Delta$ -4 desaturase and the LBLOX of SEQ ID NO:2.

It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides. The specification provides no guidance with regard to the making of variants and mutants of SEQ ID NO:2 or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would

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require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polynucleotides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of polynucleotides of SEQ ID NO:1 encoding a polypeptide having at least 60% or 80% amino acid sequence identity to SEQ ID NO:2 because the specification does not establish: (A) regions of the encoded LBLXO structure which may be modified without affecting LBLOX activity or its ability to target foreign proteins to lipid bodies; (B) the general tolerance of LBLOX to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful; (E) the specification is also silent regarding the final activity of fusion proteins of SEQ ID NO:2.

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The claims also broadly encompass not only polynucleotides encoding LBLOX and enzymes of fatty acid/lipid metabolism, but polynucleotides encoding polypeptides having any function or having no function. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The specification does not teach how to make variants of polynucleotides of SEQ ID NO:1 or polynucleotides of fatty acid/lipid metabolism encoding polypeptides having any function. The function of a polypeptide cannot be predicted from its structure and the specification does not teach how to use polypeptides having any function or having no activity. The quantity of experimentation in this area is extremely large since there is significant variability in the activity of the polynucleotides in the claims. It would require significant study to identify the actual function of the encoded polypeptides and identifying a use for the encoded polypeptide would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is known regarding the function, it is entirely unpredictable what function and activity will be found for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the encoded polypeptides.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotide comprising variants and mutants of any polynucleotides of fatty acid/lipid metabolism and any mutants and variants of SEQ ID NO:1 encoding polypeptides having any structure and any function. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of variants or mutants of SEQ ID NO:1 and polynucleotides of fatty acid/lipid metabolism having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that the claims meet the enablement requirement because one of ordinary skill in the art would be able to arrive at sequences having 80% homology, by using computer programs. Examiner respectfully disagrees. First, the claims are also drawn to polynucleotides having 60% sequence identity to SEQ ID NO:1. Second, the claims are drawn to polynucleotides having any structure, any or all any or all mutants, variants and recombinants having 60-80% sequence identity to SEQ ID NO:1, and encoding polypeptides having any activity or no activity. As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and

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guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation. Hence the rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1-4, 6, 8-9 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kindl et al., Murphy et al. and Cronan et al. (see rejection under 35 U.S.C. 112, 2<sup>nd</sup> paragraph for interpretation of "derivative" of SEQ ID NO:1).

Claims 1-4, 6, 8-9 and 10-14 are drawn to a polynucleotide encoding a protein comprising a  $\Delta$ -4 desaturase and a variant of LBLOX of SEQ ID NO:2, vector comprising said polynucleotide and *S. cerevisiae* comprising said polynucleotide.

Kindl (form PTO-1449 – Naturforsch. 52, 1997:1-8) teaches a lipid body lipxygenase (page 2, 3<sup>rd</sup> paragraph). This enzyme has been cloned by Hohne et al. (form PTO-1449 – Eur. J. Biochem. 241, 1996: 6-11 and form PTO-892 - NCBI Accession CAA63483.1) and the polynucleotide encoding residues 1-244 of said LBLOX is 100% identical to the polypeptide of SEQ ID NO:2, the teachings of which are incorporated into the reference of Kindl (page 2, 3<sup>rd</sup> paragraph). Kindl teaches that LBLOX is synthesized and transported to lipid bodies at the beginning of lipid body mobilization, during which fatty acids/lipids are metabolized (page 1, 3<sup>rd</sup> paragraph and page 7, 2<sup>nd</sup> paragraph).

The difference between the reference of Kindl et al. and the instant claims is that the reference of Kindl et al. does not teach a polynucleotide encoding a fusion protein comprising a  $\Delta$ -4 desaturase and a variant of LBLOX of SEQ ID NO:2, vectors comprising said polynucleotide or microorganism comprising said polynucleotide.

Ohlrogge et al. (form PTO-892 - Oils-Fats-Lipids 1995) teaches a polynucleotide encoding a  $\Delta$ -4 desaturase, which is an enzyme of fatty acid/lipid metabolism (abstract).

Needs elaboration of  
teachings

Yamamoto et al. (form PTO-892 – U.S. Patent No. 5,506,120) teaches a polynucleotide encoding a fusion protein, linking proteins via a regulatory signal, vectors comprising said polynucleotide and a *Saccharomyces cerevisiae* comprising said polynucleotide (abstract and Columns 5-14).

Therefore, combining the teachings of the above references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a polynucleotide encoding a fusion protein comprising the LBLOX protein of Kindl and a fatty acid/lipid metabolism enzyme of interest, such as the desaturase of Ohlrogge et al., using the method taught by Yamamoto et al. One of ordinary skill in the art would have been motivated to make the polynucleotide encoding a fusion protein in order to target an enzyme involved in fatty acid/lipid metabolism to lipid bodies and thereby direct the enzyme to the site where its activity is desired. One of ordinary skill in the art would have had a reasonable expectation of success in making the polynucleotide since making polynucleotides encoding fusion proteins is well known in the art, as taught by Yamamoto et al. One of ordinary skill in the art would have had a reasonable expectation of success in targeting the fusion protein to the lipid body since Kindl teaches that LBLOX are transported to lipid bodies.

Therefore, Kindl, Ohlrogge et al. and Yamamoto et al. render claims 1-4, 6, 8-9 and 10-14 *prima facie* obvious to those skilled in the art.

In response to the previous Office Action, applicants have traversed the above rejection.

If Yamamoto et al.  
does not teach targeting of  
enzymes then this rejection should  
be withdrawn.  
The question does not answer  
skilled in art why one  
motivated to  
make such a  
fusion protein

Art Unit: 1652

Applicants argue that applicants' invention is related to a method of targeting protein involved in lipid or fatty acid biosynthesis into liposomes or lipid bodies. The claims, however, are drawn to a polynucleotide and not a method of targeting proteins, and the claims do not recite targeting proteins to liposomes or lipid bodies.

Applicants also argue that Kindl et al., Ohlrogge et al. nor Yamamoto et al. disclose a process for targeting fusion proteins as presently claimed and therefore the references standing alone or in combination, fail teach or suggest the instant claims.

I agree

Examiner respectfully disagrees. The claims are not drawn to a process for targeting fusion proteins, but to a polynucleotide encoding a fusion protein. Also, Kindl teaches that LBLOX is synthesized and transported to lipid bodies at the beginning of lipid body mobilization, during which fatty acids/lipids are metabolized. With the teaching of Kindl et al. at hand, One of ordinary skill in the art would have been motivated to make the polynucleotide encoding a fusion protein comprising LBLOX in order to target an enzyme involved in fatty acid/lipid metabolism to lipid bodies and thereby direct the enzyme to the site where its activity is desired. Therefore, in combining the teachings of the references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a polynucleotide encoding a fusion protein comprising the LBLOX protein of Kindl and a fatty acid/lipid metabolism enzyme of interest, such as the desaturase of Ohlrogge et al., using the method taught by Yamamoto et al.

But still what is the motivation to put specifically AA desaturase

↓  
You have

to come up with a reason for such a motivation here either from Kindl or Yamamoto.

None of the claims are allowable.

So reconsider



Art Unit: 1652

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak  
Patent Examiner 1652

Manjunath Rao  
Primary Patent Examiner 1652